ORIGINAL ARTICLE

Eastern Journal of Medicine

East J Med 28(4): 698-706, 2023
DOI: 10.5505/ejm.2023.42492

What is the Role of Arterial and Venous Doppler Deteriorations in Predicting Neonatal Outcomes in Growth-restricted Fetuses?

Ceren Sağlam[1*], Ayşe Ender Yumru[2], Yunus Emre Purut[3]

[1]*Department of Obstetrics and Gynecology, Division of Perinatology, University of Health Sciences İzmir Tepecik Training and Research Hospital, İzmir, Turkey*
[2]*Department of Obstetrics and Gynecology, University of Health Sciences İstanbul Gaziosmanpasa Training and Research Hospital, İstanbul, Turkey*
[3]*Department of Obstetrics and Gynecology, Division of Gynecologic Oncology, Van Training And Research Hospital, Van, Turkey*

ABSTRACT

The study aims to evaluate the performing fetal arterial and venous Doppler to detect the optimal time for delivery in growth-restricted fetuses and its effect on perinatal outcomes.
Forty-five pregnant women with intrauterine growth restriction were included in the study. Fetal umbilical artery (UA), middle cerebral artery (MCA), and ductus venosus (DV) Doppler measurements were performed. Fetuses were investigated in three groups: normal Doppler findings, only arterial Doppler abnormality, and venous Doppler abnormality. Cord arterial gas was analyzed at the time of delivery. Neonatal information and complications (Apgar score, neonatal intensive care unit (NICU) necessity, mechanical ventilation, respiratory distress syndrome (RDS), necrotizing enterocolitis (NEC), and intraventricular hemorrhage (IVH)) were noted.
Totally 45 growth-restricted fetuses consist of 15 (%33,3) normal Doppler findings, 22 (%48,8) abnormal arterial Doppler findings, and 8 (%17,7) abnormal venous Doppler findings. There was a statistically significant difference between the abnormal venous Doppler group and the normal Doppler group when compared for gestational age at delivery, birth weight, emergent cesarean section due to fetal distress, acidosis, neonatal complications (NICU necessity, mechanic ventilation time, RDS, NEC, İVH) ($p<0,05$). As well, there was a strong correlation between gestational age and duration of both NICU stay and mechanical ventilation.
Several parameters should be performed for the surveillance and then the optimal delivery timing of growth-restricted fetuses. Our study supports that venous Doppler investigation is more predictive for fetal well-being and perinatal outcomes than the mild deterioration of the umbilical artery and middle cerebral artery.

Keywords: Intrauterine growth retardation; fetal growth restriction; Doppler; cord blood gas; neonatal outcome

Introduction

About 10% of all pregnancies in the general population have fetal growth restriction (FGR), a frequent pregnancy problem (1). After prematurity, FGR is the second most common reason of perinatal mortality and is associated with perinatal complications such as low Apgar score, hypoxemia, and cord blood acidemia, which has potentially negative effects on neonatal outcomes (2, 3). Infants having FGR are more likely to experience problems including respiratory problems, polycythemia, anemia, hypoglycemia, IVH, NEC, and hypothermia (4, 5). There is a lot of evidence showing the existence of inadequate placentation in pregnancies complicated by FGR (6, 7). The ideal protocol and optimal labor induction time in the follow-up of these fetuses are still controversial situations (8, 9). During antenatal follow-up (such as Doppler ultrasonography, biophysical profile (BPP), and non-stress test (NST)) few studies have been performed, to establish optimal delivery timing to minimize iatrogenic neonatal mortality/morbidity associated with prematurity and in utero fetal death risk (8, 10).

In our research, the aim was to make an evaluation regarding the contribution of prenatally

*Corresponding Author: Ceren Sağlam, Department of Obstetrics and Gynecology, Division of Perinatology, University of Health Sciences İzmir Tepecik Training and Research Hospital, 35180, Izmir, Turkey
E-mail: drcerensaglam@yahoo.com, Tel: +90 533 498 48 45
ORCID ID: Ceren Sağlam: 0000-0001-6013-6602, **Ayşe Ender Yumru:** 0000-0001-6449-1839, **Yunus Emre Purut:** 0000-0001-5779-3847
Received: , Accepted:

performed UA, MCA, and DV flow findings of fetuses with growth retardation to the timing of delivery and its relationship with cord blood gas values obtained at birth and neonatal complications.

Material and Method

45 individuals who were diagnosed with FGR and delivered between May 2016 and September 2017 in the University of Health Sciences Sisli Hamidiye Etfal Training and Research Hospital Gynecology and Obstetrics Department were included in this research. All patients gave their informed permission. Demographic data, ultrasonographic data, and Doppler parameters of all patients were recorded and evaluated prospectively. According to the Doppler parameters, the patients were classified into three groups with normal Doppler findings (n=15), abnormal arterial Doppler findings (n=30), and abnormal venous Doppler findings (n=8).

The gestational age of the participants included in the research was calculated in accordance with the date of the last menstrual period and verified by ultrasonographic measurements performed in the early gestational period, and calculated by crown-rump length (CRL) in whom did not know the last menstrual period. Patients whose gestational age could not be determined exactly and who did not have a first-trimester ultrasound measurement were not included in the study. Fetal weight was determined ultrasonographically in all cases by using the measurements of abdominal circumference, femur length, head circumference, and, biparietal diameter. Amniotic fluid index (AFI) was evaluated in all cases. Fetuses with birth weights below the 10th percentile were diagnosed with FGR. All ultrasonographic examinations and measurements were performed by a single practitioner using the Siemens Acuson X300 ultrasound device. A 4 MHz convex probe was used in the examinations. UA, MCA, and DV Doppler measurements were conducted in supine and slightly left lateral position. During the measurement of all Doppler indices, attention was paid to ensuring the absence of fetal respiration, movement, and uterine contraction. The waveforms were obtained when remained constant for at least five cardiac cycles. Measurements were made from three different cycles and their averages were calculated. UA Doppler measurements were made from the umbilical cord's free-floating loop in a far location from the fetus and placenta. After the vascular structure of the Willis polygon was determined with the help of color coding, Doppler indices of MCA were measured from the one closest to the probe with an insonation angle of 0 degrees. The arterial system was evaluated as abnormal in fetuses with UA pulsatility index (PI) and systolic/diastolic flow ratio (S/D) values above the 95th percentile according to the gestational age; absent or reversed end diastolic flow (A/REDF) in the umbilical artery; MCA PI below the 5th percentile and/or cerebroplacental ratio (CPR) below the 2.5th percentile. PI and systolic/atrial flow ratio (S/A) values in the ductus venosus above the 95th percentile according to the gestational age were evaluated as an abnormal venous system. All measurements were made in the last two weeks before the delivery.

Immediately after the delivery of the baby and clamping of the umbilical cord and before removing the placenta, the umbilical artery was detected. Approximately 2-3 cc of blood was taken into the heparinized syringe, and blood gas measurement was performed within 10 minutes at the latest. The umbilical artery PH values under 7.20 were considered acidosis. Apgar scores of 5-minute and 1-minute were noted.

The statistical analysis of the research's findings was done using the SPSS (Statistical Package for Social Sciences) application. *OneWayAnova* (variance analysis test) and *Tukey* posthoc tests were employed to evaluate the research data for those with equal variances and normal distribution; tests of *Mann Whitney U* and *Kruskal Wallis* were employed for those with non-normal distribution and unequal variances to compare the meaning of numerical data between the groups. *The test chi-Square* was employed for comparing the meaning of qualitative data. The results were evaluated at the $p<0.05$ significance level and the confidence interval of 95%.

The protocols of research were authorized by the Ethics Committee of Health Sciences University of Sisli Hamidiye Etfal Training and Research Hospital Clinical Research (Ethical approval no: 864).

Results

There was a homogeneous distribution among the groups with regard to parity number, body mass index, and smoking. Maternal age did not create a statistically significant difference among the samples. Birth weight was the lowest in the group with abnormal venous Doppler findings (Table1).

Table 1. Distribution of the Groups For Maternal Age and Birth Weight

Doppler findings		N	Minimum	Maximum	Mean	SD	Median
Normal Doppler flow	Maternal age	15	19	36	26,33	4,99	25
	Birth weight	15	1075	2700	1901	566,3	1835
Abnormal arterial Doppler	Maternal age	22	18	37	27,64	5,78	26,5
	Birth weight	22	738	2500	1523,5	543,45	1520
Abnormal venous Doppler	Maternal age	8	22	35	27,88	4,85	28,5
	Birth weight	8	603	1915	1142	494,6	982,5

Table 2. Distribution Between The Groups According To Gestational Age At Birth

	N	Mean ± STD	Levene Test	P value	Tukey		
					Normal Doppler flow	Abnormal arterial Doppler	Abnormal venous Doppler
Normal Doppler flow	15	35,2±3	0,999	0,011		0,199	0,008
Abnormal arterial Doppler	22	33,36±3,17			0,199		0,145
Abnormal venous Doppler	8	30,88±3,27			0,008	0,145	

While no statistically significant difference between the group with abnormal arterial Doppler and the groups with abnormal venous Doppler and normal Doppler flow according to the gestational age at birth was observed; there was a statistically significant difference between the abnormal venous Doppler group and the normal Doppler flow group (p:.008) (Table2).

There was no statistically significant difference between the abnormal arterial Doppler sample and the normal Doppler sample for NST reactivity (p-value 0.231); statistically significant differences were found between the group with abnormal venous Doppler and the groups with normal Doppler (p: 0.008) and abnormal arterial Doppler (p: 0.020) (Table 3).

A statistical difference was found between the groups according to AFI (p: 0.038), and the oligohydramnios rate was found to increase from the normal Doppler group to the abnormal venous Doppler group. Accordingly, there was no statistical difference between the group with abnormal arterial Doppler and the groups with normal Doppler and abnormal venous Doppler (p: 0.401 and 0.071, respectively), and the oligohydramnios rates of the abnormal venous Doppler group was significantly higher than the normal Doppler group (p: 0.039) (Table 3).

In terms of fetal distress, there were statistically significant differences between the group with abnormal venous Doppler (75% (6/8)) and the groups with normal Doppler (20% (3/15)) and abnormal arterial Doppler (22.7% (5 /22)) (p: 0.017 and 0.015, respectively) (Table 3).

When the birth weights were compared, although there was no statistical difference between the group with abnormal arterial Doppler and the groups with normal Doppler and abnormal venous Doppler, a statistically significant difference was found between the abnormal venous Doppler and normal Doppler groups (Graph 1) (p: 0,007).

Table 3. Distribution Between The Groups According to NST, Oligohydramnios, and Fetal Distress

	Normal Doppler flow	Abnormal arterial Doppler	Abnormal venous Doppler	TOTAL
NST				
Deceleration	3	5	6	14
Non-reactive	2	8	2	12
Reactive	10	9	0	19
Oligohydramnios				
Yes	5	9	6	20
No	10	13	2	25
Fetal distress				
Yes	3	5	6	14
No	12	17	2	31
TOTAL	15	22	8	45

Table 4. Distribution of the Groups According to Umbilical Artery PO2 and PCO2 Values

PCO2					Tukey		
	N	Mean ± STD	Levene Test	P value	Normal Doppler flow	Abnormal arterial Doppler	Abnormal venous Doppler
Normal Doppler flow	15	42.28±4,10	0,217	0,001		0,057	0,001
Abnormal arterial Doppler	22	46,76±5,98			0,057		0,051
Abnormal venous Doppler	8	52,40±7,01			0,001	0,051	
PO2							
Normal Doppler flow	15	20.24±2,61	0,343	0,000		0,221	0,000
Abnormal arterial Doppler	22	18,10±4,51			0,221		0,007
Abnormal venous Doppler	8	13,11±3,36			0,000	0,007	

There was no statistically significant difference between the groups for 1 and 5-minute Apgar scores. When evaluated in terms of umbilical artery PH and PCO2 values there was no statistical difference between the group with abnormal arterial Doppler and the groups with normal Doppler and abnormal venous Doppler; however, a statistically significant difference was found between the abnormal venous Doppler and normal Doppler groups (p: 0,005; 0,001, respectively). PH values were determined as 7,34±0,04; 7,31±0,05; 7,26±0,07 in the normal Doppler, abnormal arterial Doppler, and abnormal venous Doppler groups, respectively (Graph 2) (Table 4).

Table 5. Distribution Between The Groups According to NEC, IVH, and RDS

	Normal Doppler flow	Abnormal arterial Doppler	Abnormal venous Doppler	TOTAL
NEC				
Yes	15	20	5	40
No	0	2	3	5
IVH				
Yes	15	21	6	42
No	0	1	2	3
RDS				
Yes	13	16	1	30
No	2	6	7	15

Table 6. The Distribution Between The Groups According to Mortality and NICU Necessity

	Normal Doppler flow	Abnormal arterial Doppler	Abnormal venous Doppler	TOTAL
Neonatal death				
No	15	22	6	43
Yes	0	0	2	2
NICU necessity				
No	8	6	0	14
Yes	7	16	8	31
TOTAL	15	22	8	45

For PO2 values any statistical difference was not noted between the abnormal arterial and normal Doppler groups. There were lower PO2 values in the abnormal venous Doppler group than in the groups of abnormal arterial and normal Doppler (p:0,007; 0,000, respectively) (Table 4).

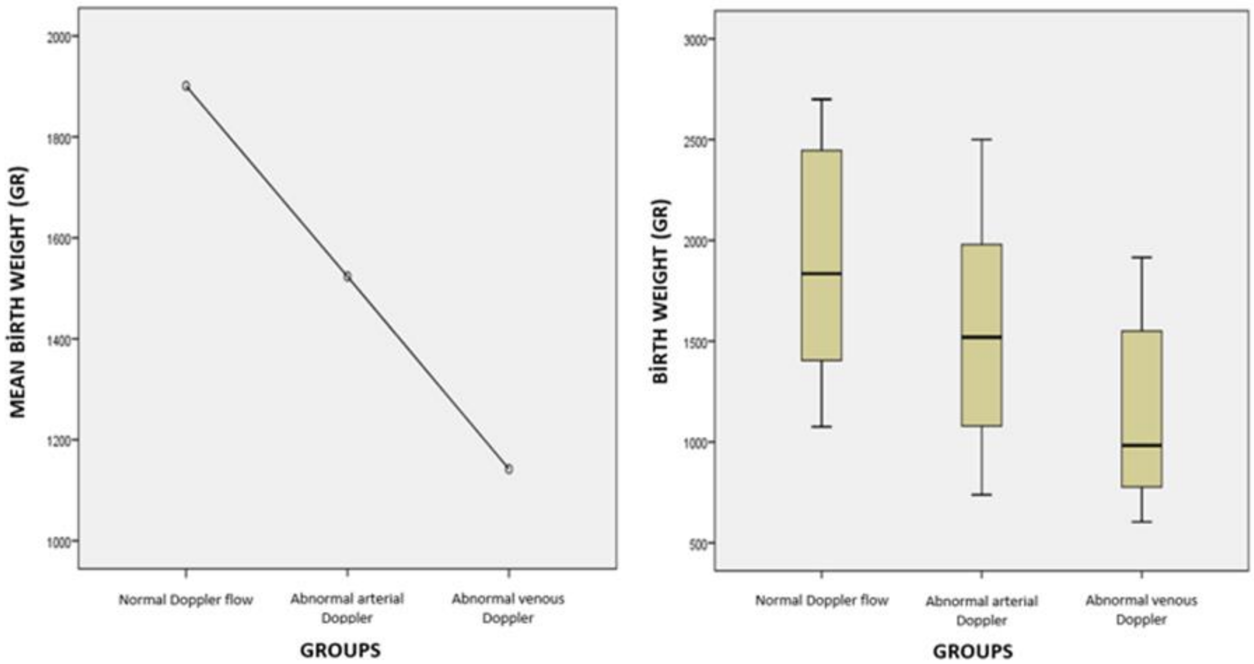
There were no cases of NEC and IVH in the normal Doppler group. For both NEC and IVH, there were no differences between the abnormal arterial Doppler and abnormal venous Doppler groups (p: 0,102; 0,166, respectively). According to the number of infants with RDS, there was a significantly higher proportion in the abnormal venous Doppler group than in the abnormal arterial Doppler and normal Doppler groups (p: 0,005; 0,001, respectively) (Table 5).

While no neonatal death was seen in normal Doppler and abnormal arterial Doppler groups, 2 fetuses (%25) with abnormal venous Doppler died in the neonatal period. All of the infants grouped in abnormal venous Doppler in the antenatal period needed NICU. Duration of NICU stay was significantly higher in the abnormal venous Doppler group (8 infants) when compared with the infants needed NICU in the normal Doppler (7 infants) and abnormal arterial Doppler (16 infants) groups (Table 6).

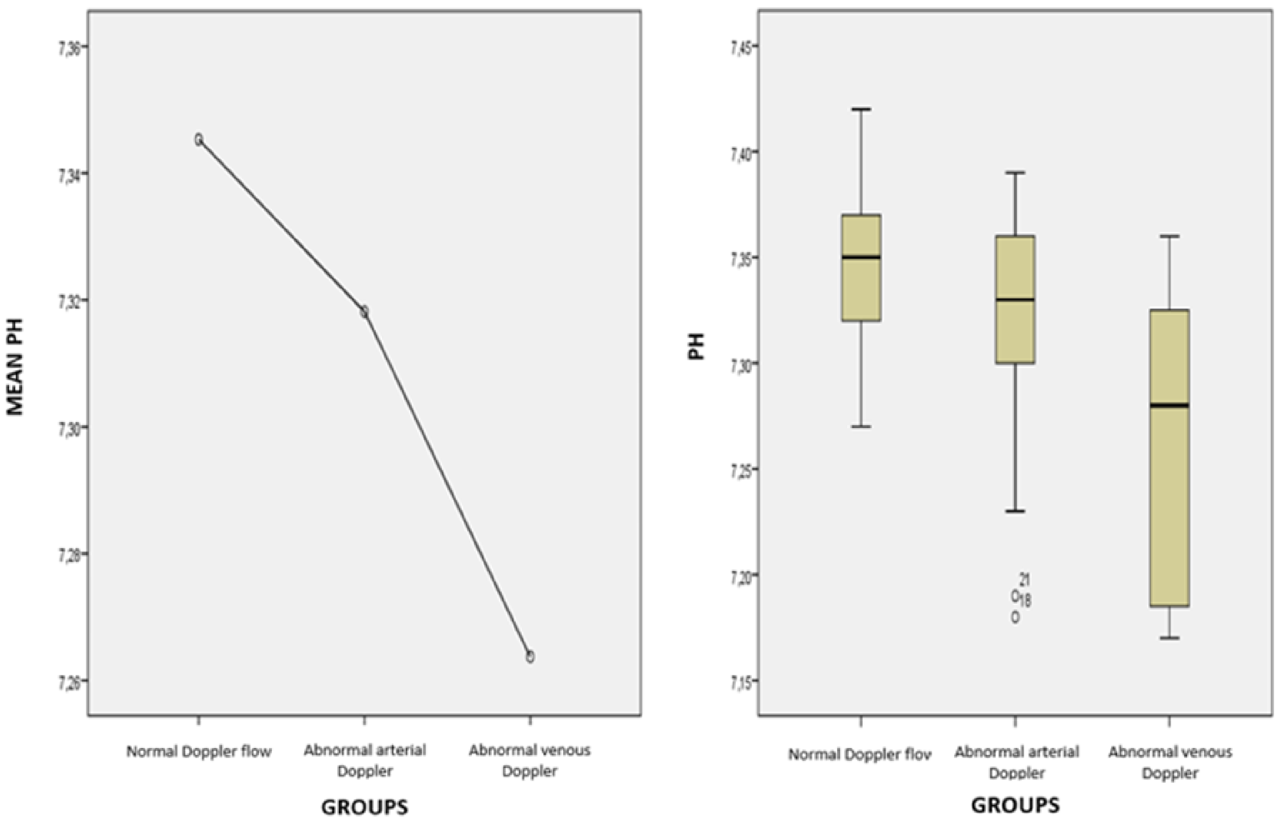
Discussion

Studies evaluating the antenatal follow-up of pregnancies complicated by FGR are quite heterogeneous. Revealing and comprehending its pathophysiology is also in continuous development and change. Antenatal follow-up using more than one modality is required in order to increase the chance of predicting neonatal outcomes and cord blood pH in growth-restricted fetuses at birth with placental insufficiency (11).

A decrease in MCA resistance, an increase both in umbilical artery resistance, and in venous blood flow to the brain are characterized by a brain-sparing effect. Those “early responses” turn into late-onset Doppler abnormalities including A/REDF in the umbilical artery, absent/reversed a wave in inferior vena cava and ductus venosus, and umbilical vein pulsation (12, 13, 14). However, there are also studies stating that measurements of MCA and UA have showed a weak correlation with perinatal outcomes (15). For all these reasons, the clinician's decision in the



Graph 1. Distribution Between The Groups For Birth Weight



Graph 2. Distribution of the Groups According To Umbilical Artery PH

follow-up of a fetus with suspected FGR will be under the influence of many variables.

Abnormal DV waveforms can be seen in hypovolemic and hypoxemic fetuses. An absent or a reversed wave in the DV is an indicator of poor prognosis and is correlated with a high rate of perinatal mortality and morbidity (12, 16, 17, 18). *Hecher et al*. reported that 5 of 8 fetuses with the absent or reverse flow in the DV died on the day they were born (12). *Rizzo et al*. showed that the

DV peak velocity and systolic/atrial peak velocity ratio were significantly higher in fetuses with FGR. It has been shown that perinatal outcomes are much worse in cases with a S/A ratio above the 95% confidence interval (19). In another recent study it was found that absent/reverse "a" wave in DV increased the odds ratio of perinatal death, fetal death, neonatal death, RDS, and abnormal pH (19.89, 18.06, 12.50, 8.29, and 9.67, respectively) and DV Doppler was a reliable tool for prediction of fetal metabolic status (20).

In our study, the DV PI and S/A ratio were above the 95th percentile and there was no absent/reversed wave in DV or pulsatility in the umbilical vein in any fetus in that abnormal venous Doppler group. From this point of view, our study investigated the deterioration in venous Doppler indices, which is the previous stage, not the absence or reversed wave, which is an indicator of severe fetal deterioration, and 2 of 8 fetuses in the group with venous Doppler dysfunction were lost in the neonatal period. However, no intrauterine loss was observed in any of the groups.

As a result of observational and randomized studies, gestational age is the most powerful factor in unfavorable neonatal outcomes in pregnancies complicated with FGR (13, 14, 21). In a study by *Baschat et al.* comparing 121 growth-restricted fetuses, gestational age at the time of delivery was found to be lower in the groups with abnormal venous Doppler finding and brain-sparing effect than the group with abnormal umbilical arterial Doppler finding (14). In our study, it was found that the gestational age at birth was significantly lower in the abnormal venous Doppler sample than the normal Doppler sample ($p<.05$), and neonatal outcomes were always against this group.

Hofstaatter et al. reported there was no association between the perinatal outcomes and the abnormal venous Doppler findings except for 1-minute Apgar scores (22). In another investigation, no significant difference was reported among Doppler groups with regard to Apgar scores (14). In our study, there was no statistically significant difference between the samples for 1 and 5-minute Apgar scores. The Apgar score of all fetuses of 5-minute with normal Doppler was 6 and above.

The predictive values of abnormal ductus venosus waveform for hospitalization to NICU, major neonatal morbidity, neonatal intubation necessity, and umbilical artery PH value below 7.1 were reported as 81,5%; 26%; 48% and 55%, respectively in the research by *Figueras et al.* (23). In the study by *Baschat et al.*, the arterial PH value of cord gas was statistically significantly lower in the group with impaired venous Doppler compared to the two groups with impaired umbilical artery Doppler and brain sparing effect (7.22 ± 0.08; 7.27 ± 0.06; 7.28 ± 0.07, respectively), arterial PO2 value was found to be statistically significantly lower in the group with impaired venous Doppler compared to the group with brain sparing effect (19.5 ± 12.2; 19.9 ± 8.8), and no significant difference was observed between the groups in arterial PCO2 values (14). In our study, the umbilical artery PH and mean PO2 value were lower and the PCO2 value was found to be higher in the group with the abnormal venous flow.

In a study, it was found that the amniotic fluid index (AFI) decreased after abnormal venous Doppler findings occurred in fetuses with only abnormal umbilical artery Doppler finding at the beginning and normal AFI. In the same study which showed significant deterioration in arterial and venous Doppler in the last examination before delivery (86.4% absent/reversed end-diastolic flow in umbilical artery, 81.8% abnormal venous Doppler), fetuses delivered by cesarean section had unreliable fetal status (54.6%), fetal intolerance/distress during labor (21.2%), and positive contraction stress test (CST) (9.1%) (24). In our study, a statistical difference was found between the groups according to amniotic fluid ratios. It was observed that the rate of oligohydramnios increased from the group with normal Doppler to the group with impaired venous system, and the rate of emergency cesarean section was significantly higher in the group with impaired venous Doppler parameters due to fetal distress.

In the study of *Ferrazzi et al.*, it was stated that Doppler deterioration was not observed in more than 50% of fetuses with abnormal fetal heart rate patterns (25). In our study, it was observed that the rates of deceleration and nonreactivity in NST tracing increased from the group with normal Doppler to the group with impaired venous flow, while the rate of reactivity decreased.

In the research of *Baschat et al.*, it was stated that most of the newborns in the sample with brain-sparing effect and impaired venous system were admitted to the NICU, and the duration of NICU stay was longest in the group with abnormal ductus venosus Doppler which had lower gestational age at birth. Respiratory complications requiring long-term mechanical ventilation and circulatory failure were most common in the abnormal ductus venosus group, and the frequency of IVH was higher in the groups with brain-sparing effect and abnormal ductus venosus. As a result of multi-regression analysis performed in the same study, gestational age at birth showed the strongest association for all postpartum complications. This relationship was strongest for RDS and weakest for IVH or NEC development (14).

The necessity for NICU was seen in the whole group with the impaired venous system in our study. In the group with normal Doppler findings and impaired arterial flow, the primary determinant of neonatal complications such as RDS, bronchopulmonary dysplasia, and IVH was gestational age, while other factors are birth weight and degree of growth retardation. It was observed that the rate of RDS was higher and the birth weight was lower in the group with the impaired venous flow, and none of the newborns with normal Doppler findings developed NEC, IVH, and sepsis.

From the point of view of FGR, Doppler parameters can be an important predictor in determining the management of pregnancy and predicting obstetric outcomes. Venous Doppler abnormality is more associated with poor prognosis. Studies with a larger number of patients are needed.

References

1. Lausman A, Kingdom J, Maternal Fetal Medicine C. Intrauterine growth restriction: screening, diagnosis, and management. J Obstet Gynaecol Can. 2013;35(8):741-8.
2. Zeitlin J, El Ayoubi M, Jarreau PH, et al. Impact of fetal growth restriction on mortality and morbidity in a very preterm birth cohort. J Pediatr. 2010;157(5):733-9 e1.
3. Turan OM, Turan S, Berg C, et al. Duration of persistent abnormal ductus venosus flow and its impact on perinatal outcome in fetal growth restriction. Ultrasound Obstet Gynecol. 2011;38(3):295-302.
4. Brar HS, Rutherford SE. Classification of intrauterine growth retardation. Semin Perinatol. 1988;12(1):2-10.
5. Soothill PW, Nicolaides KH, Campbell S. Prenatal asphyxia, hyperlacticaemia, hypoglycemia, and erythroblastosis in growth retarded fetuses. Br Med J (Clin Res Ed). 1987;294(6579):1051-3.
6. Khong TY, De Wolf F, Robertson WB, Brosens I. Inadequate maternal vascular response to placentation in pregnancies complicated by pre-eclampsia and by small-for-gestational age infants. Br J Obstet Gynaecol. 1986;93(10):1049-59.
7. Pijnenborg R, Vercruysse L, Hanssens M. The uterine spiral arteries in human pregnancy: facts and controversies. Placenta. 2006;27(9-10):939-58.
8. Baschat AA, Odibo AO. Timing of delivery in fetal growth restriction and childhood development: some uncertainties remain. Am J Obstet Gynecol. 2011;204(1):2-3.
9. Boers KE, Vijgen SM, Bijlenga D, et al. Induction versus expectant monitoring for intrauterine growth restriction at term: randomised equivalence trial (DIGITAT). BMJ. 2010;341:c7087.
10. Walker DM, Marlow N, Upstone L, et al. The Growth Restriction Intervention Trial: long-term outcomes in a randomized trial of timing of delivery in fetal growth restriction. *Am J Obstet Gynecol*. 2011;204(1):34.e1-34.e349. doi:10.1016/j.ajog.2010.09.019
11. Turan S, Turan OM, Berg C, et al. Computerized fetal heart rate analysis, Doppler ultrasound and biophysical profile score in the prediction of acid-base status of growth-restricted fetuses. Ultrasound Obstet Gynecol. 2007;30(5):750-6.
12. Hecher K, Campbell S, Doyle P, Harrington K, Nicolaides K. Assessment of fetal compromise by Doppler ultrasound investigation of the fetal circulation. Arterial, intracardiac, and venous blood flow velocity studies. Circulation. 1995;91(1):129-38.
13. Baschat AA. Doppler application in the delivery timing of the preterm growth-restricted fetus: another step in the right direction. Ultrasound Obstet Gynecol. 2004;23(2):111-8.
14. Baschat AA, Gembruch U, Reiss I, Gortner L, Weiner CP, Harman CR. Relationship between arterial and venous Doppler and perinatal outcome in fetal growth restriction. Ultrasound Obstet Gynecol. 2000;16(5):407-13.
15. Kessous R, Aricha-Tamir B, Weintraub AY, Sheiner E, Hershkovitz R. Umbilical artery peak systolic velocity measurements for prediction of perinatal outcome among IUGR fetuses. J Clin Ultrasound. 2014;42(7):405-10.
16. Gudmundsson S, Tulzer G, Huhta JC, Marsal K. Venous Doppler in the fetus with absent end-diastolic flow in the umbilical artery. Ultrasound Obstet Gynecol. 1996;7(4):262-7.
17. Kiserud T, Eik-Nes SH, Blaas HG, Hellevik LR. Ultrasonographic velocimetry of the fetal ductus venosus. Lancet. 1991;338(8780):1412-4.
18. Indik JH, Chen V, Reed KL. Association of umbilical venous with inferior vena cava blood flow velocities. Obstet Gynecol. 1991;77(4):551-7.
19. Rizzo G, Arduini D, Romanini C. Inferior vena cava flow velocity waveforms in appropriate- and

small-for-gestational-age fetuses. Am J Obstet Gynecol. 1992;166(4):1271-80.

20. Ozyüncü O, Saygan-Karamürsel B, Armangil D, et al. Fetal arterial and venous Doppler in growth restricted fetuses for the prediction of perinatal complications. *Turk J Pediatr*. 2010;52(4):384-392.
21. Bilardo CM, Wolf H, Stigter RH, et al. Relationship between monitoring parameters and perinatal outcome in severe, early intrauterine growth restriction. Ultrasound Obstet Gynecol. 2004;23(2):119-25.
22. Hofstaetter C, Gudmundsson S, Dubiel M, Marsal K. Ductus venosus velocimetry in high-risk pregnancies. Eur J Obstet Gynecol Reprod Biol. 1996;70(2):135-40.
23. Figueras F, Martinez JM, Puerto B, Coll O, Cararach V, Vanrell JA. Contraction stress test versus ductus venosus Doppler evaluation for the prediction of adverse perinatal outcome in growth-restricted fetuses with the non-reassuring non-stress test. Ultrasound Obstet Gynecol. 2003;21(3):250-5.7.
24. Baschat AA, Gembruch U, Harman CR. The sequence of changes in Doppler and biophysical parameters as severe fetal growth restriction worsens. Ultrasound Obstet Gynecol. 2001;18(6):571-7.
25. Ferrazzi E, Bozzo M, Rigano S, et al. Temporal sequence of abnormal Doppler changes in the peripheral and central circulatory systems of the severely growth-restricted fetus. Ultrasound Obstet Gynecol. 2002;19(2):140-6.